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BEFORE THE BOARD OF APPEALS AND INTERFERENCES
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Rine et al.

Serial No. 09/165,460

Filed: November 3, 1998

For: *AFC1 and RCE1: Isoprenylated CAAX Processing Enzymes*

Group Art Unit: 1652

Examiner: Ramirez, D.

Attorney Docket No.B96-021-3

CERTIFICATE OF MAILING
I hereby certify that this corr. is being deposited with the US Postal Service as First Class Mail in an envelope addressed to the Comm. for Patents, Washington, D.C. 20231 on Feb 28, 2002.

Signed _____
Richard Osman

BRIEF ON APPEAL

The Honorable Board of Appeals and Interferences
United States Patent and Trademark Office
Washington, D.C. 20231

Dear Honorable Board:

This is an appeal from the 8/31/01 rejection of claims 31, 33-35, 37-39, 41-43 and 45-46.

REAL PARTY IN INTEREST

The real party in interest is The Regents of the University of California

RELATED APPEALS AND INTERFERENCES

Appellants are unaware of any related appeals or interferences.

STATUS OF THE CLAIMS

Claims 31, 33-35, 37-39, 41-43 and 45-46 are pending and subject to this appeal.

STATUS OF THE AMENDMENTS

An amendment canceling dependent claims 32, 36, 40 and 44 to limit issues on appeal

was filed on 1/24/02. Accordingly, all Amendments are believed to be properly before the Board.

SUMMARY OF THE INVENTION

A major class of peripheral membrane proteins, known as prenylated proteins, are modified by isoprenoids on a so-called $CAaa_1Aaa_2Xaa$ (CAAX) motif, wherein C is cysteine, Aaa_1 and Aaa_2 are aliphatic amino acids and Xaa is any amino acid. This tetra-peptide sequence is located at the proteins' carboxyl termini and triggers a series of modification reactions. Specification, p.1, lines 25-29.

The presence of the $CAaa_1Aaa_2Xaa$ motif sequence targets the protein for at least 3 post-translational modifications: prenylation of the cysteine amino acid, proteolytic removal of the terminal three amino acids (*i.e.*, the Aaa_1Aaa_2Xaa tripeptide) and methylesterification of the prenylated cysteine, *i.e.*, the C-terminus. Specification, p.2, lines 7-11.

It has been determined that prenylation of the CAAX motif is essential for the proper functioning of every prenylated protein that has been tested to date. However, the functional requirement of CAAX proteolysis has not been rigorously evaluated because the gene encoding the protease has been elusive. Unfortunately, elucidation of the complete yeast genome in the absence of functional information for each yeast gene is insufficient for identification of any particular gene. Although many predicted open reading frames (ORFs) have been identified, it is not known whether these ORFs encode functional mRNAs. Specification, p.2, lines 17-25.

The present disclosure describes the discovery of two families of genes which encode polypeptides that mediate the proteolytic removal of an AAX tripeptide from a prenylated CAAX protein in a cell; the families are represented by the genes *AFC1* and *RCE1* which encode the polypeptides Afc1p and Rce1p, respectively. Accordingly, the invention provides expression vectors comprising an expressed polynucleotide that encodes a CAAX protease and hybridizes under stringent conditions to a disclosed *AFC1* and *RCE1* (SEQ ID NO:1 and SEQ ID NO:2). Specifcation, p.3, lines 10-20.

The subject expression vectors are used to make Afc1p and Rce1p for disclosed protease inhibitor drugs screens, e.g. inhibiting the proteolytic removal of an AAX tripeptide from a

prenylated CAAX protein in a cell. Specification, p.4, lines 10-12.

ISSUES

I. WHETHER CLAIMS 31, 33-34, 39, 41-42 ARE PATENTABLE UNDER 35USC103(a)

II. WHETHER CLAIMS 35, 37-38, 43 and 45-46 ARE PATENTABLE UNDER 35USC103(a)

GROUPING OF THE CLAIMS

For Issue I, the subject claims shall stand together as a group.

For Issue II, the subject claims shall stand together as a group.

ARGUMENT

I. CLAIMS 31, 33-34, 39, 41-42 ARE PATENTABLE UNDER 35USC103(a)

The Examiner's rejection of claims 31, 33-34, 39 and 41-42 over Rose et al. (GenBank Accession No. Z49617) in view of Nozaki et al. (US Pat No. 4,997,767) is not in compliance with the notice requirement of 35USC132, which requires reason and information and references useful in judging the propriety of the rejection.

The Examiner's art rejection is applied to claims reciting SEQ ID NOS:1 and 2 and relies on Rose, M. et al. (GenBank Database, Accession No. Z49617), which is dated Aug 11, 1997, more than a year after our Aug 7, 1996 priority date, and is hence not prior art. The Examiner has hand-written on the NCBI printout "Public Availability: 10/6/95". Upon telephone inquiry, the Examiner indicated that the support for his hand-written comment was a "creation-date" annotation associated with the GenBank entry; however, the same annotation continues that the entry was updated on Aug 11, 1997.

The creation date of an EMBL or GenBank record is not the public availability date. The creation date is the date the record was originally created. Frequently, these records are maintained in secrecy until a predetermined publication or patent filing date is effected. Furthermore, the creation date often does not reflect the record as subsequently published. Like

most electronic databases, Genbank and EMBL are constantly updating, amending, annotating and otherwise supplementing their records. These newer "editions" retain the creation date of the original record, but were obviously not in existence at that date. Here, the Examiner seeks to rely on a creation date for a record that could not logically have existed on that creation date. A document (electronic or otherwise) that makes explicit reference to dates and events in 1997 could not logically have been "published" or made "publically available" in 1995. This rejection is akin to citing a year 2002-updated article in the Encyclopedia Brittanica and relying on the encyclopedia's year 1768 original publication date.

To assist the Examiner, we previously provided highlighted copies of EMBL and GenBank database information for submitters (including information on withholding public availability of records after submission and record creation). We also provided the Examiner with a Sample GenBank Record explaining that even the date of last modification may not correspond to the release date.

The Examiner apparently seeks to shift the burden to Applicants to prove that Rose et al. is not prior art. We believe this position untenable as imposing an inherently impossible proof on the Applicants, and misconstruing the duty of the Examiner, which is to allow our claims unless she can establish a prima facie case of non-patentability, which includes showing that the cited art is prior art. Here, the uncontroverted evidence unequivocally demonstrates that what is cited was not what was publically available as of Oct 6, 1995.

We also previously noted that the entire yeast genome had been largely sequenced prior to the filing of our patent application, including the identification of thousands of potential ORFs. However, the sequence of the yeast genome is just an inherent property of the prior art genome itself, and provides no more suggestion for isolating, recombinantly expressing and using a particular gene than does the unsequenced yeast geneome. Furthermore, computer-predicted ORFs are not even known to encode functional mRNA and even if such ORFs contained a sequence similar to that required by our expression vectors, the claimed vectors would be neither anticipated nor obvious. Our expression vectors do not encompass any natural yeast chromosome and require that the recited coding sequence be operatively joined to a promoter. In the absence of any evidence for function, there would be no motivation to select out one of the

thousands of potential yeast ORFs of unknown function, isolate what may or may not be a coding sequence, and operatively join it to a promoter in an expression vector.

II. CLAIMS 35, 37-38, 43 and 45-46 ARE PATENTABLE UNDER 35USC103(a)

The Examiner's rejection of claims 35, 37-38, 43 and 45-46 over Lye et al. (GenBank Accession No. Z49260) in view of Nozaki et al. is not in compliance with the notice requirement of 35USC132, which requires reason and information and references useful in judging the propriety of the rejection.

The art rejection applied to claims 35-38 and 43-46 (reciting SEQ ID NOS:3 and 4) relies on Lye, et al. (GenBank Database, Accession No. Z49260), which is also dated Aug 11, 1997, more than a year after our Aug 7, 1996 priority date, and is hence not prior art. Instead of a publication date, the Examiner appears to rely on a purported unpublished submission date. This is improper; if a database entry does not recite a publication date, it can not be relied upon as prior art; see MPEP2128. The Action offers no evidence that the relied upon sequence was published at any time prior to Aug 11, 1997.

We previously noted that the entire yeast genome had been largely sequenced prior to the filing of our patent application, including the identification of thousands of potential ORFs which were not even known to encode functional mRNA. What Lye discloses are computer predictions of thousands of possible CDS regions. A computer is programmed to input raw genomic sequence, select all possible CDS regions over 100 codons, and then exclude those that are more than 50% overlapped by a larger predicted CDS. The authors promise that CDS regions of the initial dataset subsequently eliminated by the algorithm are nevertheless "available upon request." In addition, the disclosure provides algorithm-predicted PROSITE database matches, though the authors caution that some of these may be "fortuitous".

Lye does not disclose any gene or gene product, but the results of a first run effort to sequence the entire XIII chromosome of Saccharomyces cerevisiae. That natural yeast XIII chromosome is, of course, prior art, and Lye provides no more than an inherent property of that chromosome - its sequence. Lye discloses no more than raw genomic data weighted by a computer for thousands of possible genes and genetic elements. The Examiner uses our own

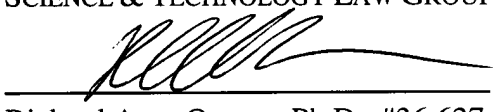
disclosure to select out one of these and uses our own disclosure to provide motivation to recombine it in an expression vector. In the absence of any evidence for function, there would have been no motivation to select out one of the thousands of yeast ORFs of unknown function, isolate what may or may not be a coding sequence, and operatively join it to a promoter in an expression vector, as expressly required by our claims.

Absent a prior art suggestion that SEQ ID NO:1 or 3 encodes a protein of determined function sufficient to motivate the isolation, cloning and expression of such SEQ ID NO using techniques such as those of the cited Nozaki et al. (US Pat No 4,997,767) and Sambrook, J. et al. (Mol. Cloning, Cold Spring Harbor Press, p. 16.3-16.16) references, the claims are in compliance with 35USC102 and 103.

Appellants respectfully request reversal of the pending Final Action by the Board of Appeals.

We petition for and authorize charging our Deposit Account No.19-0750 all necessary extensions of time. The Commissioner is authorized to charge any fees or credit any overcharges relating to this communication to our Dep. Acct. No.19-0750 (order B96-021-3).

Respectfully submitted,
SCIENCE & TECHNOLOGY LAW GROUP



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CLAIMS ON APPEAL

31. A recombinant expression vector comprising a promoter operably linked to an expressed polynucleotide which encodes a polypeptide and hybridizes under highly stringent conditions to a nucleic acid consisting of SEQ ID NO:1, wherein said polypeptide mediates the proteolytic removal of an AAX tripeptide from a prenylated CAAX protein and said highly stringent conditions comprise hybridization and wash conditions selected to be 5° C lower than the thermal melting point (Tm) for said nucleic acid at a defined ionic strength and pH.

33. A vector according to claim 31, wherein the polypeptide comprises SEQ ID NO:2.

34. A vector according to claim 31, wherein the polypeptide consists of SEQ ID NO:2.

35. A recombinant expression vector comprising a promoter operably linked to an expressed polynucleotide which encodes a polypeptide and hybridizes under highly stringent conditions to a nucleic acid consisting of SEQ ID NO:3, wherein said polypeptide mediates the proteolytic removal of an AAX tripeptide from a prenylated CAAX protein and said highly stringent conditions comprise hybridization and wash conditions selected to be 5° C lower than the thermal melting point (Tm) for said nucleic acid at a defined ionic strength and pH.

37. A vector according to claim 35, wherein the polypeptide comprises SEQ ID NO:4.

38. A vector according to claim 35, wherein the polypeptide consists of SEQ ID NO:4.

39. A recombinant cell transduced with the vector of claim 31.

41. A recombinant cell transduced with the vector of claim 33.

42. A recombinant cell transduced with the vector of claim 34.

43. A recombinant cell transduced with the vector of claim 35.

45. A recombinant cell transduced with the vector of claim 37.

46. A recombinant cell transduced with the vector of claim 38.